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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,268	04/11/2006	Alexandra Babarina	14836-49926	1125

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,268	BABARINA ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-10 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-10 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1 and 4-6 have been amended. Claims 1-10 are pending and under consideration.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is vague and indefinite in the recitation of "other channels being charged with the same medium". It is unclear where, in the muti-channel instrument, the medium comprising the cytostatic or cytotoxic agent is to be analyzed. For purpose of examination the "other channel being charged with the same medium" will be read as other channels being charged with the medium comprising the cytostatic or cytotoxic substance.

The term "lengthy" and "short" in claim 8 are relative terms which renders the claim indefinite. The terms "lengthy" and "short" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Section 2173 of the M.P.E.P. states

Claims Must Particularly Point Out and Distinctly Claim the Invention

The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent..

In the instant case, the specification does not provide a limiting definition for a "lengthy" or "short" time which would provide a boundary between that which is "lengthy" and "short" versus that which is not lengthy or short, or "of medium length". Thus, a potential infringer

would not be able to ascertain when a time interval was large enough not to be considered lengthy or short , and therefore outside the scope of the claims..

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Metzger et al (Toxicology, 2001, Vol. 166, pp. 97-108, reference of the IDS submitted May 6, 2005) in view of Freshney (Culture of Animal Cells, Third Edition, 1994, pages 83, and pages 86-87, cited in the previous Office action), Parce et al (Science, 1989, Vol. 246, pp. 243-247), Hafeman et al (U.S. 5,766,875) and Hafner (Biosensors and Bioelectronics, 2000, Vol. 15, pp. 149-158, reference of the IDS filed May 6, 2005).

Claim 1 is drawn to a medium for measuring the efficacy of a tumor therapy on single cell suspensions, comprising the essential amino acids, vitamins, salts and carbon donors, characterized in that the medium comprises from 0.1 to 1 mM buffer of pH 7 to 7.4; 4 to 6 g/l glucose; and 2 to 5mM glutamine as a carbon source and 5 to 20% fetal calf serum. Claim 2 embodies the method of claim 1 characterized in that it comprises phosphate buffer as a buffer. Claim 3 embodies the medium of claim 1 or 2, characterized in that it comprises from 8 to 12% fetal calf serum. Claim 6 is drawn to a method comprising determining the acid formation by single cell suspensions of tumor cells in the medium of claim 1 in the presence and absence of a substance having cytostatic activity. Claim 7 embodies the method of claim 6 wherein acid formation is carried out by means of a pH electrode on which the single cell suspension is immobilized within the flow cell. Claim 8 embodies in part, the method of claim 6 wherein the medium is pumped through a flow cell until a baseline reading is obtained and the acidification is measured at short intervals, and the measurement cycle is repeated over a lengthy period. Claim 9 embodies the method of claim 8 wherein the acidification of the medium is measured every 1.5

min to 2 min, and the measurement cycle is repeated over 14 to 24 hrs. Claim 10 embodies the method of claim 9 wherein the method is carried out in a multi-channel instrument with one channel being charged by the medium without the cytostatic agent and the other channels being charged with the medium containing the cytostatic agent.

Metzger et al teach that malignant cell lines were grown in DMEM comprising 10% fetal calf serum (page 100, first column, lines 2-3) Metzger et al teach that tissue samples including tumor tissue were placed in modified RPMI and processed to obtain a single cell suspension (page 100, second column, first full paragraph). Metzger et al teach that cells were then seed into special capsules in order to measure metabolic rate in the presence of chemotherapeutic drugs , and that the RPMI was low-buffered with 1mM phosphate (page 101, first column, lines 4-16). Metzger et al teach that the microflow chambers were set up in parallel and that tumor cell acidification was measured along with that of controls that had not been exposed to drugs (page 101, first column, lines 1-11), thus fulfill the specific embodiment of claim 10 requiring a multi-channel instrument. Metzger et al teach that the flow cell comprises a Cytosensor-Microphysiometer system within the flow cell which uses light addressable sensors to detect milli pH changes (pages 100-101, bridging paragraph). Hafner provides evidence that when a voltage is applied to the Cytosensor Microphysiometer, an electric field is created therein which will be affected by the pH of the bathing medium (page 151, second column, lines 9-19 of Section 3.1), and thus the teachings of Metzger et al regarding flow cell comprises a Cytosensor-Microphysiometer meet the limitation of claim 7 regarding a pH electrode. Metzger et al teach that perfusion was stopped every 90 seconds for the measurement of acidification (page 101, first column, lines 11-16) and the accumulation of acidification data over 17 or18 hours (Figures 1 and 2) which meets the limitation of claim 9. Metzger et al did not teach the DMEM was used in the measurement of acidification.

Parce et al teaches that reducing the buffer capacity of a growth medium to ~1mM increases the pH change of the medium for a given excretion of acid by the cells and under conditions of a closed system, no drift in pH would be expected to occur due to equilibration with atmospheric CO2 and that metabolic rates are detected by determining acidification rates. Parce et al also teach that normal cell culture medium is used, including serum (page 244, right column, lines 12-28).

Freshney teaches that Dulbecco's Modification Medium (DMEM) (pages 86-87) comprises 4.5g/L glucose and 584 mg/L glutamine (4mM glutamine) which meets the specific limitations of the claims. Freshney also teaches that transformed cells grow better at ph 7.0 to 7.4 (page 83, first paragraph under "pH"), which meets the limitation of claim 1 requiring pH 7.0 to 7.4.

Hafemann et al teach a modified RPMI for measurement of extracellular acidification. Hafemann et al teach also teach that Modified Dulbecco's Medium can be used for the measurement of extracellular acidification (column 15, lines 18-27).

It would have been prima facie obvious at the time the claimed invention was made to use with DMEM with 10% FCS with the exception that the only buffer was phosphate buffer at 1mM concentration. One of skill in the art would have been motivated to do so by the teachings of Parce et al on the use of normal growth medium including serum, the teachings of Freshney on the constituents of DMEM, the teachings of Hafemann et al regarding the alternative use of DMEM in place of RPMI for the measurement of extracellular acidification and the teachings of Parce et al suggesting that only the buffering capacity of the medium should be altered so that said medium is a low buffering medium of 1mM phosphate.

All claims are rejected.

All other rejections and objections as set forth in the prior Office action are withdrawn in light of applicants amendments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/
Primary Examiner, Art Unit 1643